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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/771,263	01/26/2001	Gale Arthur Granger	IRVN-005CIP	7988

24353 7590 10/20/2004

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EXAMINER	
YAEN, CHRISTOPHER H	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/771,263	THOMPSON ET AL.	
	Examiner	Art Unit	
	Christopher H Yaen	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-5,7-14,17-24 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-5,7-14,17-24 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Re: Granger *et al*
Priority Date: 17 March 1995

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/30/2004 has been entered.

2. Claims 1,6,15-16, and 25 are canceled without prejudice or disclaimer, claims 2-5,7-14,17-24 and 26 are pending.

3. Claims 2-5,7-14,17-24, and 26 are examined on the merits.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Applicants have switched inventions from product claims to method claims. In an interview with the applicant (see interview of 9/2/2004), it was agreed to that a switch was permissible because the switch would simplify the issues of the application. Applicant cited section MPEP section 819.01 as evidence that a switch was at the discretion of the examiner. As a result, all rejections made of record are withdrawn with regard to the product claims and the case will be examined as method claims.

Claim Rejections - 35 USC § 112, 2nd paragraph

6. Claims 2-5,7-14,17-22 and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. In particular, claims 19, 20, and dependent claims thereof recite the term "unrelated" as part of the invention. The specification has not defined the extent of unrelatedness. It is unclear if the term relates to familial or genetic relatedness and as such, the metes and bounds of the term cannot be determined.

8. With regard to claims 21 and 22 in the recitation of the term "stimulated", it is unclear as to what extent of stimulation is intended. Because the type of stimulation has not been defined in the specification, the metes and bounds of the term cannot be determined.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 2-5,7-14,17-24, and 26 rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,203,787. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the claims are overlapping and cover the same scope of invention. The claims of the instant invention are drawn to a method of treating cancer or eliciting an anti-tumor response in a patient comprising the administration of alloactivated lymphocytes from a donor that is unrelated to the patient. The claims of US Patent 6,203,787 are drawn to a method of either eliciting an anti-tumor immunological response (claim 15) or a method of treating a tumor in a human patient (claim 16) of which both comprise the administration of allogeneic cells that have been co-cultured in the presence of other allogeneic cells so as to alloactive the cells. Absent evidence to the contrary, the cells administered in the `787 patent are the same as those being administered in the instant invention.

11. Claims 21-22,24, and 26 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-34 of U.S. Patent No. 6,207,147. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of claims in the US patent encompass the claims of the instant invention. The claims of the instant invention are drawn to a method of treating cancer comprising the administration to a patient a composition comprising a stimulated lymphocyte and a tumor associated antigen (TAA). Claims 21-23, 25-26, and 28-34 of US patent 6,207,147 are drawn to a method of inducing an anti-tumor immune response comprising the administration of an

immunogeneic composition comprising stimulated lymphocytes and a tumor associated antigen. Thus one of ordinary skill in the art would have found it *prima facie* obvious to treat a tumor comprising the administration of an immunogeneic composition which comprises stimulated lymphocytes and TAAs.

Claim Rejections - 35 USC § 102

12. Claims 2-5,8-10,13,17,19-20 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Kohler *et al* (Cancer Immunol. Immunother. 1988, 26(1):74-82, previously cited).

The specification states that the source of the donor cells are "unrelated human donors allogeneic to the subject to be treated" (see page 15, line 13). Furthermore, the term allogeneic is conventionally understood in the art as "[t]wo or more individuals (or strains) are stated to be allogeneic to one another when the genes at one or more loci are not identical in sequence in each organism" (see http://medical-dictionary.com/dictionaryresults.php). Therefore, for the purposes of this rejection, the term "unrelated" will be interpreted as being genetically unrelated due to differences in genes at one or more loci.

Kohler *et al* teach the administration of alloactivated lymphocytes for the purpose of eliciting an anti-tumor response (claim 20) or for the purposes of treating a tumor (claim 19) through a treatment modality known as adoptive chemotherapy or ACIT (see page 74). Although the donor cells are initially isolated from a healthy haploidentical donor (which is interpreted here as individuals who have familial relations, but differ in

sequence by at least one or more loci), the cells from the haploidentical donor are mixed with allogeneic cells from at least 10 different human donors (claims 2-4), wherein the lymphocytes in either case are inactivated by irradiation(claim 5) (see page 75, 2nd column). Kohler *et al* also teach that the PBLs isolated from the patient express high levels of OK-IA, which is the HLA-DR molecule, which suggests that the cells that were alloactivated expressed the HLA-DR molecule (claim 8) (see pages 77, 79 2nd column and figure 4). It is also taught that the alloactivated lymphocytes are co-cultured with allogeneic cells for a duration of time that enables them to elicit an immune response (claim 9), and extend life expenctancy (claim 10). The specification of the instant invention teaches that the culture period must be at least 12 hours (see page 18, line 20) whereas, Kohler *et al* teach that the cells are co-cultured for at least 6 days (claim 13). Kohler *et al* additionally teach that the alloactivated cells are administered to a patient via i.v. infusion (see page 75, 2nd column), which is encompassed by claim 17 which recites administration via an injection needle. Finally, because the alloactivated cells are administered via i.v. infusion and because the patients described by Kohler *et al* have various types of malignant diseases (see table 2), depending on the patient in question, such administration would encompass administration of the alloactivated cells at distal sites.

Claim Rejections - 35 USC § 103

13. Claims 2-4,7,9-10,13,17-24, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kruse *et al* (PNAS USA 1990, 87(24):9577-9581) cited in applicant

IDS #DE). For the purposes of this rejection, the term "unrelated" will be interpreted as donor cells that are allogeneic to the patient.

a. Kruse *et al* teach a method of eliciting an immune response and a method of treating a cancer comprising the method of administering alloactivated lymphocytes that are derived from an unrelated patient or are allogeneic donor cells (see page 9578 1st column). Furthermore, it is disclosed that the composition comprising the allogeneic cells co-administered with inactivated 9L gliosarcoma cells which presumably would have tumor associated antigens, and hence would express such antigens on the surface of the tumor cell. Because the donor lymphocytes are obtained from a strain of rats (specifically DA rats) any number of rats could have been used to obtain the lymphocytes. Kruse *et al* also disclose the culture of the lymphocytes with the stimulator cells was for a time that was sufficient to elicit an anti-tumor response and for a time sufficient to reduce tumor mass (see page 9579, 1st column in particular), wherein the time is about 5 days (see page 9578, 1st column). It was also disclosed that the lymphocytes were administered via an injectable means (see page 9578, 2nd column), wherein the composition of cells was administered at or around the site of the tumor (see page 9578, 2nd paragraph).

b. Kruse *et al* do not specifically teach a method of administering an alloactivated lymophocyte composition to humans.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to adapt the method for human therapy because Kruse *et*

al provide the motivation and expectation of success in doing so because when the alloactivated cells where administered to a mouse model, there was a reduction in the amount of tumor burden. More specifically, Kruse *et al* taught a method of administering alloactivated lymphocytes that were allogeneic to the patient in the presence of tumor cells that had been inactivated. One of ordinary skill in the art would have been motivated to perform the claimed methods in humans because the animal model used by Kruse *et al* would have provided sufficient motivation and predictability to perform in humans because it was shown by Kruse *et al* that the method was effective and capable of eliciting or treating cancer. The modification of the method from rats to human would flow logically from the teachings of Kruse *et al* because the animal model used is representative of human disease (see page 9580 and page 9581 1st column). Furthermore, depending on the number of donor cells needed, one of skill in the art would find it obvious to obtain more donor patients from which cells can be obtained because as taught by Kruse *et al* the allogeneicity of the cells elicits a stronger reaction (see page 9580).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen
Art Unit 1642
October 15, 2004

GARY NICKOL
PRIMARY EXAMINER